

Page 61, line 11, after "Sequence" insert -- (SEQ ID Nos. 38-43) --.

Please amend the specification by replacing the original Sequence Listing pages 62-72 with the attached revised Substitute Sequence, pages 62-76. Please further amend the specification by renumbering pages 73-81 to follow consecutively after the Substitute Sequence Listing.

IN THE CLAIMS

Please cancel pending claim 1 without prejudice and insert therefor the following new claims:

--53. A method for producing a product polypeptide, comprising the steps of:

(1) culturing a host cell transformed with a replicable expression vector, the replicable expression vector comprising DNA encoding a product polypeptide operably linked to a control sequence capable of effecting expression of the product polypeptide in the host cell; wherein the DNA encoding the product polypeptide has been obtained by a method comprising the steps of:

(a) constructing a family of variant replicable plasmids comprising a transcription regulatory element operably linked to a gene fusion encoding a fusion protein; wherein the gene fusion comprises a first gene encoding a polypeptide and a second gene encoding at least a portion of a phage coat protein, wherein the variant replicable plasmids comprise variant first genes encoding polypeptides;

(b) transforming suitable host cells with the plasmids;

(c) infecting the transformed host cells with an amount of helper phage encoding the phage coat protein sufficient to produce recombinant phagemid particles wherein no more than about 20 percent of the phagemid particles display one or more copies of the fusion protein on the surface of the phagemid particles;

(d) culturing the transformed infected host cells under conditions suitable for forming recombinant phagemid particles containing at least a portion of the plasmid and capable of transforming the host cells;

(e) contacting the recombinant phagemid particles with a target molecule so that at least a portion of the phagemid particles bind to the target molecule;

(f) separating phagemid particles that bind to the target molecule from those that do not bind;

(g) selecting one of the variant polypeptides displayed on a phagemid particle from step (f) as the product polypeptide; cloning DNA encoding the product polypeptide into the replicable expression vector; and

(2) recovering expressed product polypeptide.

54. The method of claim 53, further comprising infecting suitable host cells with the phagemid particles that bind or do not bind and repeating steps (d) through (f).

55. The method of claim 54, wherein the steps are repeated one or more times.

56. The method of claim 53, wherein the expression vector further comprises a secretory signal sequence.

57. The method of claim 53, wherein the transcription regulatory element is a promoter system selected from the group consisting of lac Z, pho A, tryptophan, tac, lambdaPL, bacteriophage T7, and combinations thereof.

58. The method of claim 53, wherein the product polypeptide is a mammalian protein.

59. The method of claim 58, wherein the product polypeptide is an antibody or binding fragment thereof.

60. The method of claim 59, wherein the product polypeptide comprises an antibody Fab portion.

61. The method of claim 58, wherein the product polypeptide is a human protein.

62. The method of claim 53, wherein the product polypeptide comprises more than about 100 amino acid residues.

63. The method of claim 53, wherein the phage coat protein is M13 phage gene III coat protein or M13 phage gene VIII coat protein.

64. The method of claim 63, wherein the phage coat protein is M13 phage gene III coat protein.

65. The method of claim 53, wherein the conditions are adjusted so that no more than 10% of phagemid particles display one or more copies of the fusion protein on the surface of the particle.

66. The method of claim 53, wherein the amount of phagemid particles displaying more than one copy of the fusion protein on the surface of the particles is less than 20% of the amount of phagemid particles displaying a single copy of the fusion protein.

67. The method of claim 53 wherein the number of phagemid particles displaying more than one copy of the fusion protein on the surface of the particle is less than about 10% of the amount of phagemid particles displaying a single copy of the fusion protein.

68. The method of claim 53, wherein the number of phagemid particles displaying more than one copy of the fusion protein is less than 1% of the phagemid particles displaying a single copy of the fusion protein.

69. The method of claim 53, wherein the conditions are adjusted so that the number of fusion proteins per recombinant phagemid particle is about 0.1 (number of bulk fusion proteins/number of phagemid particles).

70. The method of claim 53, wherein the gene fusion comprises a DNA triplet encoding an mRNA suppressible terminator codon between the first gene encoding a polypeptide and the second gene encoding at least a portion of a phage coat protein.

71. The method of claim 53, wherein the helper phage is selected from the group consisting of M13KO7, M13R408, M13-VCS, and Phi X174.

72. The method of claim 53, wherein the helper phage is M13KO7 and the coat protein is the M13 phage gene III coat protein.

73. The method of claim 53, wherein the host cells are *E. coli*.

74. The method of claim 53, wherein the variant replicable plasmids do not contain a further gene encoding a mature phage coat protein.

75. The method of claim 53, wherein the variant replicable plasmids do not contain a complete phage genome.

76. A product polypeptide produced by the method of Claim 53.

77. A method for producing a product polypeptide, comprising the steps of:

(1) culturing a host cell transformed with a replicable expression vector, the replicable expression vector comprising DNA encoding a product polypeptide operably linked to a control sequence capable of effecting expression of the product polypeptide in the host cell; wherein the DNA encoding the product polypeptide has been obtained by a method comprising the steps of:

(a) expressing in recombinant host cells variant gene fusions, each gene fusion comprising a first gene encoding a polypeptide and a second gene encoding at least a portion of a phage coat protein, the variant gene fusions encoding a family of variant fusion proteins;

(b) culturing the recombinant host cells under conditions suitable for forming recombinant phagemid particles, wherein no more than a minor amount of the phagemid particles display more than one copy of the fusion protein on the surface of the phagemid particles;

(c) contacting the recombinant phagemid particles with a target molecule so that at least a portion of the phagemid particles bind to the target molecule;

(d) separating phagemid particles that bind to the target molecule from those that do not bind;

(e) selecting one of the variant polypeptides displayed on a phagemid particle from step (d) as the product polypeptide; cloning DNA encoding the product polypeptide into the replicable expression vector; and

(2) recovering expressed product polypeptide.

78. The method of claim 77, wherein the product polypeptide is a mammalian protein.

79. The method of claim 78, wherein the product polypeptide is an antibody or binding fragment thereof.

80. The method of claim 78, wherein the product polypeptide comprises an antibody Fab portion.

81. The method of claim 78, wherein the product polypeptide is a human protein.

82. The method of claim 77, wherein the phage coat protein is M13 phage gene III coat protein.

83. The method of claim 77, wherein the conditions are adjusted so that no more than 10% of phagemid particles display one or more copies of the fusion protein on the surface of the particle.

84. The method of claim 77, wherein the amount of phagemid particles displaying more than one copy of the fusion protein on the surface of the particles is less than 20% of the amount of phagemid particles displaying a single copy of the fusion protein.

85. The method of claim 77, wherein the number of phagemid particles displaying more than one copy of the fusion protein on the surface of the particle is less than about 10% of the amount of phagemid particles displaying a single copy of the fusion protein.